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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,996	05/24/2007	Mariko Fujimura	0152-0842PUS1	2104
2292 7590 06/22/2010 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER DO, PENSEE T	
			ART UNIT 1641	PAPER NUMBER
			NOTIFICATION DATE 06/22/2010	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/587,996	Applicant(s) FUJIMURA ET AL.	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 01, 2009 has been entered.

Priority

This application, 10587996, filed 05/24/2007 is a national stage entry of PCT/JP05/01504 , International Filing Date: 02/02/2005 and claims foreign priority to 2004-026237 , filed 02/03/2004 and has a publication number of 20080131978. The effective filing date is 2/03/2004.

Amendment Entry & Claims Status

The amendment filed on January 04, 2010 has been acknowledged and entered.

Claims 1, 4-8 and newly added claim 9 and 10 are pending and being examined.

Claimed Invention

1. (Currently Amended) A labeled specific binding material comprising a substance capable of specifically binding to an analyte, a spacer and a magnetic bead having a diameter of 0.5 to 10 um, wherein the specific binding substance is coupled to the

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magnetic bead via the spacer and the spacer is polyalkylene glycol having 50 to 500 repeat units.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant amended claim 8 to recite "without stirring" which is a negative limitation and pointed to the specification for support in the paragraph [0023]. However, this is not sufficient to support such negative limitation for negative limitation requires clear support in the specification. Applicant submitted that "the magnetic bead labeled secondary antibody is dropped on the detection area and with leaving at 4 degrees C to room temperature for 5 minutes to 1 hour for it to bind to the antigen in the sample" is enough to support the negative limitation that the magnetic bead labeled secondary antibody binds to the antigen "without stirring".

This is not persuasive to support the negative limitation because "leaving the magnetic labeled secondary antibody with the antigen at 4 degrees C to room

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temperature" does not imply whether there is stirring or not. It primarily describes only the temperature and does not mention whether the mixture is stirred or not.

Therefore, this is a new matter rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson et al. (US PGPub. 2003/0092029 A1) in view of Rohr (US 5,445,970) and further in view of Thompson (US PGPub 2003/0190304).

For claim 1, Josephson teaches a composition comprising binding moieties linked to a magnetic particle. The binding moieties cause a specific interaction with a target molecule (see [58]) via functionalized polymer such as polyethylene glycol (see [24] and [61]).

However, Josephson fails to teach the magnetic particles size ranges from 0.5 to 10 um (microns).

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Rohr teaches using magnetic particles coated with a polymer coating as labels in assays. The magnetic particles have size range between 0.01 μm to 100 μm or 0.01 to 10 μm (see col. 12, lines 55-65). Rohr also discusses that "as will be appreciated by those skilled in the art, the composition, shape, size and density of magnetically attractable material may vary widely and a label can be selected based upon such factors as the analyte of interest and the desired assay protocol" (see col. 12, line 65- col. 13, line 2). Rohr further suggests that "the magnetic particles can be selected to have a specific gravity so as to tend to be suspended within the reaction mixture thereby enhancing the reactivity of the binding member. The magnetic particles can also be selected to have a specific gravity so as to tend to settle in the reaction mixture thereby enhancing the reactivity of the binding member with the immobilized reagent on the solid phase. (see col. 13, lines 3-25).

Thus, it would have been obvious to one of ordinary skills in the art to combine the teaching of Rohr and Josephson to use magnetic particles size ranges from 0.5 to 10 μm because particles of this size do not settle rapidly in solution as those larger than 10 μm nor do they require thermal agitation as those of size smaller than 0.5 μm . (see Rohr col. 13, lines 3-25). One of ordinary skills in the art would have expected reasonable success in combining these two references because both references teach magnetic particles with polymer coating for use as labels in assays.

However, Josephson and Rohr fail to teach using a polyalkylene glycol having 50 to 500 repeat units.

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Thompson teaches using a polymer such as Polyethylene glycol (PEG) as a spacer, i.e. "if two groups are linked to the polymer such as PEG, one at each end, the length of the polymer can impact upon the effective distance, and other spatial relationships, between the two groups. The polymeric portion can be of any length or molecular weight but these characteristics can affect the biological properties. Polymer average molecular weights particularly useful for decreasing clearance rates in pharmaceutical applications are in the range of 2,000 to 35,000 daltons. If the polymer is a straight chain PEG, particularly useful lengths of polymers, represented by $(Z)_n$, where Z is the monomeric unit of the polymer, include n having a range of 50-500". (See [0075]).

Since Josephson teaches using PEG as a spacer and Thompson also uses PEG as a spacer, it would have been obvious to one of ordinary skills in the art to vary the length of the PEG in Josephson to have a range of monomers from 50-500 as taught by Thompson because Thompson teaches one can vary the length of the PEG within this range of monomers to optimize or confer the desired biological activity of the two groups being linked by the PEG.

For claims 2-4, 9 Josephson teaches that polymer is polyethylene glycol or polysaccharides and derivatives (see [24] and [61]).

For claim 6, Josephson teaches that the binding moieties are antibodies and the target analytes are antigen (see [78]).

For claim 8, Josephson teaches a method of detecting a target comprising contacting such composition described above with a sample and the magnetic

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resonance (magnetic signal) is detected. (see [83] and [84]). Josephson teaches immobilizing polymer such as polysaccharide to the particles via biotin-avidin complex. In this embodiment, the polysaccharide has reactive ends which are biotinylated and then is exposed to avidin linked nanoparticles (see [119], [130]). Josephson also teaches a step of washing the unbound specific binding material. (see [96] and [141]).

Claim 5, 7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson et al. (US PGPub. 2003/0092029 A1) and further in view of Rohr and Thompson, as applied to claim 1-4, 6 and 8, and in view of Foster (US 4,444,879).

Josephson and Rohr and Thompson have been discussed above.

However, they fail to teach that the polyethylene glycol is bound to the magnetic particle via a biotin-avidin complex and packaging the composition described above into a kit.

Foster teaches packing assay reagents into a kit with instruction. (see col. 15, fig. 6).

For claims 5 and 10, although Josephson does not explicitly teaches attaching polyethylene glycol to the surface of a magnetic particles via biotin-avidin complex, Josephson teaches a method of immobilizing a polysaccharide to a nanoparticle, such polysaccharide is used the same way as the polyethylene glycol, as a spacer or linker to bind the binding moiety to the nanoparticle. (see discussion above). Thus, one of

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ordinary skills in the art would be motivated to immobilize the polyethylene glycol to the nanoparticle via a biotin-avidin complex as the polysaccharide.

For claim 7, it would have been obvious to one of ordinary skills in the art to pack the reagents used in the assay taught by Josephson combined with Rohr into a kit as taught by Foster for advantage of economic convenience and long-term storage.

Response to Arguments

Applicant's arguments filed December 1, 2009 and January 4, 2010 have been fully considered but they are not persuasive.

Applicants argue that Josephson teaches that the diameter of the magnetic particles is less than 1-100 nm and one of ordinary skill in the art would not combine Rohr with Josephson since Josephson specifically recite the desired size of the nanoparticles.

This is not found persuasive because:

Josephson teaches in paragraph [0063] that the diameter of the magnetic particles can be less than 1-100 nm or 15 nm to 200 nm. Rohr teaches that the magnetic particles range from 0.01 to 1,000 microns or 10 nm to 1000 microns. The range of diameter in Rohr includes the range of the magnetic particles in Josephson. Thus, one of ordinary skills in the art would have been motivated to combine the two references.

Regarding the newly added limitation, "without stirring", Applicants argue that Rohr does not teach such limitation because

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Rohr "970 recites:

"Generally, small magnetic particles with a mean diameter of less than about 0.03 μm (300 Angstroms) can be kept in solution by thermal agitation and do not spontaneously settle Generally, large magnetic particles having a mean diameter greater than about 10 microns can respond to weak magnetic fields. Although large or dense labels may be used, such labels may require that the reaction mixture be stirred or agitated during the incubation steps to inhibit settling of the particles. In another embodiment, the magnetic particles can be selected to remain dispersed in the reaction mixture for a time sufficient to permit the required binding reactions without the need for a stirring or mixing means (col. 13, lines 7-25)."

Applicants further interpret the above teachings in Rohr such that it indicates that the small particles with a mean diameter of less than 0.03 μm or 30 nm do not require being stirred because they do not spontaneously settle. However, the large magnetic particle requires being stirred in order to inhibit the settling of the particles. Therefore, the particles that do not require stirring in Rohr range from 0.01 μm to 0.03 μm which does not overlap with the claimed range of 0.5 μm to 10 μm . And if the larger particles are used, they must be stirred.

This is not persuasive because:

Rohr teaches that only those particles with a diameter greater than 10 μm need to be stirred, i.e. "Generally, large magnetic particles having a mean diameter greater than about 10 microns can respond to weak magnetic fields. Although large or dense

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labels may be used, such labels may require that the reaction mixture be stirred or agitated during the incubation steps to inhibit settling of the particles.” (Rohr, col. 13, lines 7-25).

Rohr also teaches that: “In another embodiment, the magnetic particles can be selected to remain dispersed in the reaction mixture for a time sufficient to permit the required binding reactions without the need for a stirring or mixing means (col. 13, lines 7-25).” Therefore, all particles with the size between 0.03 μm and 10 μm , which includes the claimed range, need not to be stirred or mixed when they are in binding reactions.

Conclusion

This is an RCE of applicant's earlier Application No. 10/587,996. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641

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/Jacob Cheu/

Primary Examiner, Art Unit 1641